

WHAT IS CLAIMED IS:

1. A method for treating CD40⁺ malignancies comprising administering a therapeutically effective amount of an antibody or antibody fragment which binds to CD40L thereby inhibiting CD40/CD40L interaction or CD40 signaling.
2. The method of Claim 1, wherein the CD40⁺ malignancy is a B-cell lymphoma or a B-cell leukemia.
3. The method of Claim 2, wherein the B-cell lymphoma is Hodgkin's Disease (HD) or Non-Hodgkin's Lymphoma (NHL).
4. The method of Claim 3, wherein the NHL is low grade, intermediate grade or high grade.
5. The method of Claim 3, wherein the NHL is selected from the subtype group consisting of: small lymphocytic, follicular and predominantly small cleaved cell, follicular and mixed small cleaved and large cell type, follicular and predominantly large cell type, diffuse small cleaved cell, diffuse mixed small and large cell, diffuse large cell, large cell immunoblastic, lymphoblastic, small non-cleaved Burkitt's and non-Burkitt's

type, AIDS-related lymphomas, angioimmunoblastic lymphadenopathy, mantle cell lymphoma, and monocytoid B-cell lymphoma.

6. The method of Claim 2, wherein the B-cell leukemia is a chronic B-cell leukemia, acute lymphoblastic leukemia of a B-cell lineage, or chronic lymphocytic leukemia of a B-cell lineage.

7. The method of Claim 2, wherein the antibody or antibody fragment which binds to CD40L is IDEC-131, 3E4, 2H5, 2H8, 4D9-8, 4D9-9, 24-31, 24-43, 89-76 or 89-79.

8. The method of Claim 7, wherein the antibody or antibody fragment is chimeric, bispecific, human or humanized.

9. The method of Claim 2, wherein the antibody fragment is Fab, Fab', scFv or F(ab')₂.

10. The method of Claim 2, further comprising administering a therapeutically effective amount of a second antibody or fragment thereof, a chemotherapeutic, a combination of chemotherapeutic agents and/or a radiotherapy.

11. The method of Claim 10, wherein the radiotherapy is external radiation treatment or a radiolabeled antibody.

12. The method of Claim 11, wherein the radiolabeled antibody is radiolabeled IDEC-131, RITUXAN®, or B1 or fragments thereof.

13. The method of Claim 12, wherein the radiolabeled antibody is radiolabeled with ¹²³I, ¹²⁵I, ¹³¹I, ¹¹¹In, ¹³¹In, ³²P, ⁶⁴Cu, ⁶⁷Cu, ²¹¹At, ¹⁷⁷Lu, ⁹⁰Y, ¹⁸⁶Re, ²¹²Pb, ²¹²Bi, ⁴⁷Sc, ¹⁰⁵Rh, ¹⁰⁹Pd, ¹⁵³Sm, ¹⁸⁸Re, ¹⁹⁹Au, ²¹¹At, and ²¹³Bi.

14. The method of Claim 10, wherein the chemotherapeutic agent for treating HD is any one or more of the following: an alkylating agent, a vinca alkaloid, procarbazine, methotrexate or prednisone.

15. The method of Claim 10, wherein the chemotherapeutic agent for treating NHL is any one or more of the following: an alkylating agent, cyclophosphamide, chlorambucil, 2-CDA, 2'-deoxycytosine, fludarabine, cytosine arabinoside, cisplatin, etoposide or ifosfamide.

16. The method of Claim 10, wherein the combination of chemotherapeutic agents for treating HD is: MOPP, ABVD, ChIVPP, CABS, MOPP plus ABVD, MOPP

plus ABV, BCVPP, VABCD, ABDIC, CBVD, PCVP, CEP, EVA, MOPLACE, MIME, MINE, CEM, MTX-CHOP, EVAP or EPOCH.

17. The method of Claim 10, wherein the combination of chemotherapeutic agents for treating NHL is: CVP, CHOP, C-MOPP, CAP-BOP, m-BACOD, ProMACE-MOPP, ProMACE-CytaBOM, MACOP-B, IMVP-16, MIME, DHAP, ESHAP, CEPP(B) or CAMP.

18. The method of Claim 10, wherein the chemotherapeutic agent for treating a B-cell leukemia is at least one of the following: anthracycline, cyclophosphamide, L-asparaginase and a purine analog.

19. The method of Claim 10, wherein the combination of chemotherapeutic agents for treating a B-cell leukemia is: vincristine, prednisone, anthracycline and cyclophosphamide or asparaginase; vincristine, prednisone, anthracycline, cyclophosphamide and asparaginase; CHOP; CMP; CVP; COP or CAP.

20. The method of Claim 10, wherein the second antibody is an anti-CD20 antibody.

21. The method of Claim 21, wherein the anti-CD20 antibody is RITUXAN® or a fragment thereof or B1 or a fragment thereof.

~~22.~~ A method of treating a CD40⁺ malignancy comprising the step of administering an anti-CD40L antibody or fragment thereof wherein the anti-CD40L antibody or antibody fragment blocks CD40-CD40L interaction or inhibits CD40 signalling; and administering an anti-CD20 antibody or fragment thereof.

23. The method of Claim 22, wherein the CD40⁺ malignancy is a B-cell lymphoma or a B-cell leukemia.

~~24.~~ A combination therapy for the treatment of a CD40⁺ malignancy comprising a CD40L antagonist and at least one of the following (a) a chemotherapeutic agent or a combination of chemotherapeutic agents, (b) a radiotherapy, (c) an anti-CD20 antibody or fragment thereof and (d) anti-CD40 antibody or fragment thereof.

25. The method of Claim 24, wherein the radiotherapy is external radiation treatment or a radiolabeled antibody.

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26. The method of Claim 25, wherein the radiolabeled antibody is radiolabeled with ^{123}I , ^{125}I , ^{131}I , ^{111}In , ^{131}In , ^{32}P , ^{64}Cu , ^{67}Cu , ^{211}At , ^{177}Lu , ^{90}Y , ^{186}Re , ^{212}Pb , ^{212}Bi , ^{47}Sc , ^{105}Rh , ^{109}Pd , ^{153}Sm , ^{188}Re , ^{199}Au , ^{211}At , and ^{213}Bi .

27. The combination therapy of Claim 24 wherein the CD40^+ malignancy is a B-cell leukemia or B-cell lymphoma.

28. The combination therapy of Claim 27, wherein the B-cell lymphoma is HD or NHL.

29. The combination therapy of Claim 28, wherein the NHL is low grade, intermediate grade or high grade.

30. The combination therapy of Claim 28, wherein the NHL is selected from the subtype group consisting of the following: small lymphocytic, follicular and predominantly small cleaved cell, follicular and mixed small cleaved and large cell type, follicular and predominantly large cell type, diffuse small cleaved cell, diffuse mixed small and large cell, diffuse large cell, large cell immunoblastic, lymphoblastic, small non-cleaved Burkitt's and non-Burkitt's type, AIDS-related lymphomas, angioimmunoblastic lymphadenopathy, mantle cell lymphoma and monocytoid B-cell lymphoma.

31. The combination therapy of Claim 28, wherein the B-cell leukemia is a chronic B-cell leukemia, acute lymphoblastic leukemia of a B-cell lineage, or chronic lymphocytic leukemia of a B-cell lineage.

32. The combination therapy of Claim 24, wherein the CD40L antagonist is an anti-CD40L antibody or a fragment thereof.

33. The combination therapy of Claim 32, wherein the anti-CD40L antibody is IDEC-131 or a fragment thereof.

34. The combination therapy of Claim 32, wherein the anti-CD40L fragment is Fab, Fab', scFv or F(ab')₂.

35. The combination therapy of Claim 24, wherein the anti-CD20 antibody is RITUXAN® or a fragment thereof or B1 or a fragment thereof.

36. The combination therapy of Claim 28, wherein the chemotherapeutic agent for treating HD is any one or more of the following: an alkylating agent, a vinca alkaloid, procarbazine, methotrexate or prednisone.

37. The combination therapy of Claim 28, wherein the chemotherapeutic agent for treating NHL is any one or more of the following: an alkylating agent, cyclophosphamide, chlorambucil, 2-CDA, 2'-deoxycytosine, fludarabine, cytosine arabinoside, cisplatin, etoposide or ifosfamide.

38. The combination therapy of Claim 28, wherein the combination of chemotherapeutic agents for treating HD is: MOPP, ABVD, ChlVPP, CABS, MOPP plus ABVD, MOPP plus ABV, BCVPP, VABCD, ABDIC, CBVD, PCVP, CEP, EVA, MOPLACE, MIME, MINE, CEM, MTX-CHOP, EVAP or BROCH.

39. The combination therapy of Claim 28, wherein the combination of chemotherapeutic agents for treating NHL is: CVP, CHOP, C-MOPP, CAP-BOP, m-BACOD, ProMACE-MOPP, ProMACE-CytaBOM, MACOP-B, IMVP-16, MIME, DHAP, ESHAP, CEPP(B), or CAMP.

40. The combination therapy of Claim 28, wherein the chemotherapeutic agent for treating a B-cell leukemia is: anthracycline, cyclophosphamide, L-asparaginase, a purine analog.

41. The combination therapy of Claim 28, wherein the combination of chemotherapeutic agents for treating a B-cell leukemia is: vincristine, prednisone,

anthracycline and cyclophosphamide or asparaginase; vincristine, prednisone, anthracycline, cyclophosphamide and asparaginase; CHOP; CMP; CVP; COP or CAP.

42. A composition for the treatment of a CD40⁺ malignancy comprising an (i) anti-CD40L antibody or antibody fragment thereof and at least one of the following: (ii) a radiolabeled antibody that binds CD40L or CD20, (iii) an anti-CD20 antibody or fragment thereof, or (iv) a chemotherapeutic agent or a chemotherapeutic combination.

43. The composition for the treatment of a CD40⁺ malignancy of Claim 42 wherein the malignancy is a B-cell lymphoma or a B-cell leukemia.

44. The composition of claim 43, wherein the B-cell leukemia is Hodgkin's Disease or NHL.

45. The composition of Claim 42, wherein the radiolabeled antibody is radiolabeled IDEC-131, RITUXAN®, or B1.

46. The composition of Claim 46, wherein the radiolabeled antibody is radiolabeled with ¹²³I, ¹²⁵I, ¹³¹I, ¹¹¹In, ¹³¹In, ³²P, ⁶⁴Cu, ⁶⁷Cu, ²¹¹At, ¹⁷⁷Lu, ⁹⁰Y, ¹⁸⁶Re, ²¹²Pb, ²¹²Bi, ⁴⁷Sc, ¹⁰⁵Rh, ¹⁰⁹Pd, ¹⁵³Sm, ¹⁸⁸Re, ¹⁹⁹Au, ²¹¹At, and ²¹³Bi.

47. The composition of Claim 44, wherein the NHL is low grade, intermediate grade or high grade.

48. The composition of Claim 44, wherein the NHL is selected from the NHL subtype group consisting of the following: small lymphocytic, follicular and predominantly small cleaved cell, follicular and mixed small cleaved and large cell type, follicular and predominantly large cell type, diffuse small cleaved cell, diffuse mixed small and large cell, diffuse large cell, large cell immunoblastic, lymphoblastic, small non-cleaved Burkitt's and non-Burkitt's type, AIDS-related lymphomas, angioimmunoblastic lymphadenopathy, mantle cell lymphoma and monocytoid B-cell lymphoma.

49. The composition of Claim 42, wherein the anti-CD40 antibody is IDEC-131 or a fragment thereof.

50. The composition of Claim 42, wherein the anti-CD20 antibody is RITUXAN® or a fragment thereof or B1 or a fragment thereof.

51. The composition of Claim 43, wherein the chemotherapeutic agent for treating HD is any one or more of the following: an alkylating agent, a vinca alkaloid, procarbazine, methotrexate or prednisone.

52. The composition of Claim 44, wherein the chemotherapeutic agent for treating NHL is any one or more of the following: an alkylating agent, cyclophosphamide, chlorambucil, 2-CDA, 2'-deoxycytosine, fludarabine, cytosine arabinoside, cisplatin, etoposide or ifosfamide.

53. The composition of Claim 44, wherein the combination of chemotherapeutic agents for treating HD is: MOPP, ABVD, CHVPP, CABS, MOPP plus ABVD, MOPP plus ABV, BCVP, VABCD, ABDIC, CBVD, PCVP, CEP, EVA, MOPLACE, MIME, MINE, CEM, MTX-CHOP, EVAP or EPOCH.

54. The composition of Claim 44, wherein the combination of chemotherapeutic agents for treating NHL is: CVP, CHOP, C-MOPP, CAP-BOP, m-BACOD, ProMACE-MOPP, ProMACE-CytaBOM, MACOP-B, IMVP-16, MIME, DHAP, ESHAP, CEPP(B), or CAMP.

55. The composition of Claim 43, wherein the chemotherapeutic agent for treating a B-cell leukemia is: anthracycline, cyclophosphamide, L-asparaginase, a purine analog.

56. The composition of Claim 43, wherein the combination of chemotherapeutic agents for treating a B-cell leukemia is: vincristine, prednisone,

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12°	13°	14°	15°	16°	17°	18°	19°	20°	21°	22°	23°	24°	25°	26°	27°	28°	29°	30°	31°	32°	33°	34°	35°	36°	37°	38°	39°	40°	41°	42°	43°	44°	45°	46°	47°	48°	49°	50°	51°	52°	53°	54°	55°	56°	57°	58°	59°	60°	61°	62°	63°	64°	65°	66°	67°	68°	69°	70°	71°	72°	73°	74°	75°	76°	77°	78°	79°	80°	81°	82°	83°	84°	85°	86°	87°	88°	89°	90°